



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,697	01/30/2002	Donald W. Petersen	06317-038003	8553

26161 7590 04/02/2003

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER

WITZ, JEAN C

ART UNIT PAPER NUMBER

1651

DATE MAILED: 04/02/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,697	PETERSEN, DONALD W.	
	Examiner	Art Unit	
	Jean C. Witz	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments

Applicant's arguments filed January 7, 2003 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 16-30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of O'Leary et al. (5,484,601), Yim et al. and WO 9840113 taken as a whole.

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant asserts that Wironen teaches away by reference to a commercially available product covered by the O'Leary patent that uses glycerol as the carrier. The quote attributed to Wironen states that the Wironen considers it "likely that this material is rapidly washed away"; however, the teaching of O'Leary is not limited to any preferred or marketed embodiments and Wironen provides only mere supposition that the material will be washed away. Applicant completely ignores the teaching of O'Leary that includes the following statement: "Thus, e.g., where the carrier component is glycerol and separation of bone powder occurs to an excessive extent where a particular application is concerned, a thickener such as a solution of polyvinyl alcohol, polyvinylpyrrolidone, cellulosic ester such as hydroxypropyl methylcellulose, carboxy methylcellulose, pectin, food-grade texturizing agent, gelatin, dextran, collagen, starch, hydrolyzed polyacrylonitrile, hydrolyzed polyacrylamide, polyelectrolyte such as polyacrylic acid salt, etc., can be combined with the carrier in an amount sufficient to significantly improve the suspension-keeping characteristics of the composition." (emphasis added.)

Applicant asserts that "Wironen discloses glycerol as a neurolytic agent, while O'Leary discloses that glycerol is the 'especially preferred' carrier." First, there is no requirement of O'Leary that the carrier component must be glycerol; again, the teaching of a U.S. Patent is not limited to its preferred embodiments. However, it is noted at page 6 of the disclosure of Wironen, at line 16, glycerol is anticipated as being included in the composition of Wironen. Therefore, Wironen is not deemed to be

teaching away from the use of glycerol and Applicant's arguments to that end are not found to be persuasive.

Applicant argues that Wironen uses a cross-linked gelatin that is disclosed as important to his invention; this teaching is simply not germane to the rejection at issue. Simply because more than one reference is used in a rejection under 35 USC 103, this in no way means that the only rejection that may be made is one where every ingredient in each disclosed invention must be combined into some resultant conglomerate composition. The Examiner pointed out in the previous office action that the disclosure of WO 9840113 is also drawn to a bone paste for the repair of bone defects. The disclosed paste contains demineralized bone matrix, an inorganic component such as ceramics hydroxyapatite and calcined bone, or bone morphogenic proteins or other growth factors and mixtures thereof. Other ingredients which may be present in the paste include wetting agents and carboxymethyl cellulose (see pages 5-6). At page 13, the reference states that the composition "may act as a carrier for cortical, cancellous or cortical and cancellous bone chips. Such compositions are useful for filling larger bone voids. In addition, when these bone chips are not demineralized, they provide an added spectrum of biological properties not exhibited by the gelatin alone or the gelatin plus the osteogenic components (i-iv)." Therefore, the disclosure of Wironen was specifically included in the rejection to teach that one of ordinary skill in the art would be aware that there is a motivation to include cancellous bone into a bone repair composition for the reasons set forth above. Applicant appears to be arguing that the disclosure of Wironen be interpreted to mean

that cancellous bone can only be included in the composition of Wironen; however, that interpretation is too limited since the benefits that the cancellous bone brings to the composition of Wironen would be expected by one of ordinary skill in the art to accrue to other bone repair compositions. O'Leary, Yim and even Wironen himself provide disclosures such as found in virtually every patent document as exemplified at page 6 of the Wironen document which states that "Other factors [followed by a list of substances] . . . or combinations thereof or any other material found to add to the desirable properties of the essential composition of this invention may be included." Statements of this type recognize that other ingredients have known benefits and may be added to disclosed compositions for their contribution to the composition in question. Therefore, there is a motivation to include the cancellous bone described by Wironen into the O'Leary composition.

Applicant further argues that there is no motivation to combine the calcium sulfate of Yim into the composition of O'Leary. Applicant asserts that the "reasons for adding calcium sulfate are either inconsistent with the type of compositions that O'Leary intended to form or have already been addressed by O'Leary." Applicant points to improving retention and reducing setup time "suggest that the composition should be relatively viscous, but then points to the embodiments of O'Leary where "the compositions are intended to be 'runny'." Applicant then asserts that where the embodiments are intended to be "like a putty", the thickener fulfills this purpose; therefore, the addition of the calcium sulfate in "unnecessarily redundant, and as a result, there is no motivation to form Applicant's claimed composition."

This argument fails to take into consideration that O'Leary envisions a range of consistencies of the composition and defines "the term 'flowable' as used herein applies to compositions whose consistencies range from those which can be described as shape-sustaining but readily deformable, e.g., those which behave like putty, to those which are runny. Specific forms of flowable bone powder compositions include cakes, pastes, creams and fillers." O'Leary et al. state at col. 1, lines 36-43 that "[I]t is a particular object of the invention to provide a composition of liquid or pastelike consistency comprising demineralized osteogenic bone powder and a biocompatible liquid synthetic organic material as a carrier for the bone powder with or without such optional ingredients as thixotropic agents, medicaments, and the like, and to apply the composition at a bone defect site to induce new bone ingrowth at the site."

Therefore the goal of the invention is to provide a composition that is a carrier for the demineralized bone powder as well as other optional ingredients. O'Leary et al. disclose at col. 2, line 53 to col. 3, line 13, that "[a]ny of a variety of substances can be introduced into the bone particles" and includes a non-limiting list which includes inorganic elements, parenchymal cells, growth factors, bone morphogenic proteins, and mesenchymal elements. " (emphasis added.) Calcium sulfate would be considered by one of ordinary skill in the art to be such an "inorganic element".

Yim specifically teaches that "[t]o reduce the preparation time and improve the above formulation's handling characteristics, [Patentees] have surprisingly found that it is desirable to add a calcium sulfate hemihydrate-containing substance (CSHS). The CSHS is preferably either pure calcium sulfate hemihydrate, also known as Plaster of

Paris (POP), or a mixture of POP and hydroxyapatite (POP:HA). Adding a CSHS reduces setup time and provides improved moldability and consistency of the resulting formulation." The "above formulation" includes osteogenic proteins and a suitable "protein-sequestering agent", disclosed at col. 7, lines 25-34, as cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), such as methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose. It is noted that Yim already includes the thickener of O'Leary yet finds that the addition of calcium sulfate improves the composition for certain applications. As a result, one of ordinary skill in the art would expect the composition of O'Leary would similarly be improved for certain applications by the inclusion of calcium sulfate, as one of ordinary skill in the art would also expect that the composition of O'Leary would be improved for certain applications by the inclusion of the cancellous bone disclosed by Wironen. There is no suggestion in the O'Leary reference that it will become inoperative with the inclusion of other ingredients and in fact, as indicated above, suggests that other ingredients may be included.

The fact that Yim chooses to administer bone morphogenic proteins as purified in solution or lyophilized is merely a selection of an obvious alternative by the inventor. Yim clearly discloses that a source of bone morphogenic proteins is demineralized bone matrix. Actually, the fact that Yim chooses purified bone morphogenic proteins over demineralized bone matrix is less germane than the disclosure of O'Leary who teaches that not only is demineralized bone matrix preferred, but also that bone morphogenic proteins may be added to the composition in addition to the

demineralized bone matrix. See O'Leary et al. col. 2, line 53 to col. 3, line 13, that "[a]ny of a variety of substances can be introduced into the bone particles" and includes a non-limiting list which includes inorganic elements, parenchymal cells, growth factors, bone morphogenic proteins, and mesenchymal elements. " (emphasis added.) Therefore, there is clearly a benefit to including both demineralized bone matrix and bone morphogenic proteins such that this disclosure provides evidence that the disclosure of Yim cannot be interpreted to require either one or the other but not both.

Therefore, the references, as a whole, certainly provide motivation to add both the calcium sulfate of Yim and the cancellous bone of Wironen to the composition of O'Leary with the expected known and disclosed benefit that both components will add to the composition of O'Leary. Both O'Leary et al. and Yim et al. have the same object in creating a malleable, workable bone growth promoting composition. One of ordinary skill in the art when reviewing the disclosure of Yim would have been motivated to include a calcium sulfate component into the composition of O'Leary et al. with the expected benefit disclosed by Yim et al., i.e. that a calcium sulfate component would add improved handling, moldability and consistency to the formulation of O'Leary as well as reducing the set up time. The compositions of Yim and O'Leary are so sufficiently similar that one of ordinary skill in the art at the time the invention was made would be aware of the properties of the calcium sulfate hemihydrate would not impair or otherwise negatively affect the components of the O'Leary composition. Both compositions contain components that provide either directly or indirectly osteogenic

Art Unit: 1651

proteins, and both compositions contain a cellulosic material which is being used for the same purpose, i.e. to impart viscosity and suspension properties to the respective compositions. The general amounts of both the demineralized bone matrix and the cellulose material are taught by the references. The optimization of the amount of calcium sulfate and mixing solution to be further included is deemed well within the skill of the practitioner at the time the invention was made as it is clear that the amount of calcium sulfate is directly related to desired rate of set up of the composition, i.e. the more calcium sulfate used, the faster the composition will set up and harden. Further, it is clear that the amount of mixing solution is inversely related to the desired set up time and directly proportional to the ultimate consistency of the composition, i.e. the more mixing solution used, the more dilute the calcium sulfate and the slower the set up time but the more liquid the composition will become.

Finally, the claims recite the further inclusion of cancellous bone. Both patents teach that other conventional components included in bone growth promoting compositions may be included in the disclosed compositions. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include cancellous bone chips into the composition of O'Leary et al. for the benefit described in the disclosure of WO 9840113, i.e. they fill larger bone voids and provide an added spectrum of biological properties to the composition.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-Th and alternate Fridays.

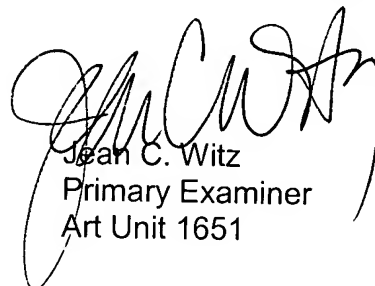
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Application/Control Number: 10/060,697

Page 11

Art Unit: 1651

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Jean C. Witz
Primary Examiner
Art Unit 1651

April 1, 2003